

CLAIMS

What is claimed is:

1. A method for reducing oxidative stress in a cell of a subject comprising contacting the
5 cell with a sulfhydryl protected glutathione prodrug so as to reduce oxidative stress in a cell.
2. The method of claim 1, wherein oxidative stress is caused by a toxic substance, a
10 pathogen, ultraviolet light, physical injury and/or genetic disease.
3. The method of claim 2, wherein the toxic substance is a drug, alcohol, metal ion,
ultraviolet light or radiation.
4. The method of claim 3, wherein the drug is acetaminophen, aminoglycoside antibiotic or
15 a chemotherapeutic drug.
5. The method of claim 2, wherein the pathogen is HIV or anthrax spores.
6. The method of claim 1, wherein reducing oxidative stress reduces injury caused by an
20 infection, cardiovascular disease, genetic disease, physical injury, ophthalmic disease,
cancer, inflammation, neuropathy, acute respiratory distress syndrome (ARDS), exposure
to a toxic substance, exposure to ultraviolet light, exposure to radiation and/or decreased
levels of glutathione.
- 25 7. The method of claim 1, wherein the sulfhydryl protected glutathione prodrug is L-CySSG,
GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable
salt thereof.

8. The method of claim 1, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
- 5 9. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 1.
10. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 1.
- 10 11. A method for reducing oxidative stress in a cell of a subject comprising contacting the cell with a sulfhydryl protected cysteine prodrug so as to reduce oxidative stress in a cell, wherein the prodrug is CySSMA.
- 15 12. The method of claim 11, wherein oxidative stress is caused by a toxic substance, a pathogen, ultraviolet light, physical injury and/or genetic disease.
13. The method of claim 12, wherein the toxic substance is a drug, alcohol, metal ion, ultraviolet light or radiation.
- 20 14. The method of claim 13, wherein the drug is acetaminophen, aminoglycoside antibiotic or a chemotherapeutic drug.
15. The method of claim 12, wherein the pathogen is HIV or anthrax spores.
- 25 16. The method of claim 11, wherein reducing oxidative stress reduces injury caused by an infection, cardiovascular disease, genetic disease, physical injury, ophthalmic disease, cancer, inflammation, neuropathy, acute respiratory distress syndrome (ARDS), exposure to a toxic substance, exposure to ultraviolet light, exposure to radiation and/or decreased levels of glutathione.

17. The method of claim 11, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
- 5 18. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 11.
19. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 11.
- 10 20. A method for increasing glutathione levels in a cell comprising administering to a subject a sulfhydryl protected glutathione prodrug so as to increase glutathione levels in a cell.
- 15 21. The method of claim 20, wherein increasing glutathione levels reduces injury caused by an infection, cardiovascular disease, genetic disease, physical injury, ophthalmic disease, cancer, inflammation, neuropathy, acute respiratory distress syndrome (ARDS), exposure to a toxic substance, exposure to ultraviolet light, exposure to radiation and/or decreased levels of glutathione.
- 20 22. The method of claim 20, wherein the sulfhydryl protected glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable salt thereof.
- 25 23. The method of claim 20, wherein administration is selected from the group consisting of aerosol, topical, intravenous, intramuscular, subcutaneous, implantable pump, continuous infusion and oral administration.
24. The method of claim 20, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.

25. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 20.
- 5 26. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 20.
27. A method for increasing glutathione levels in a cell comprising administering to a subject a sulfhydryl protected cysteine prodrug so as to increase glutathione levels in a cell,
10 wherein the prodrug is CySSMA.
28. The method of claim 27, wherein increasing glutathione levels reduces injury caused by an infection, cardiovascular disease, genetic disease, physical injury, ophthalmic disease, cancer, inflammation, neuropathy, acute respiratory distress syndrome (ARDS), exposure
15 to a toxic substance, exposure to ultraviolet light, exposure to radiation and/or decreased levels of glutathione.
29. The method of claim 27, wherein administration is selected from the group consisting of aerosol, topical, intravenous, intramuscular, subcutaneous, implantable pump, continuous
20 infusion and oral administration.
30. The method of claim 27, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
- 25 31. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 27.
32. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 27.

33. A method for increasing L-cysteine levels in a cell comprising administering to a subject a sulfhydryl protected glutathione prodrug so as to increase L-cysteine levels in a cell.
- 5 34. The method of claim 33, wherein increasing L-cysteine levels reduces injury caused by an infection, cardiovascular disease, genetic disease, physical injury, ophthalmic disease, cancer, inflammation, neuropathy, exposure to a toxic substance, exposure to ultraviolet light, acute respiratory distress syndrome (ARDS), exposure to radiation and/or decreased levels of glutathione.
- 10 35. The method of claim 33, wherein the sulfhydryl protected glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable salt thereof.
- 15 36. The method of claim 33, wherein administration is selected from the group consisting of aerosol, topical, intravenous, intramuscular, subcutaneous, implantable pump, continuous infusion and oral administration.
- 20 37. The method of claim 33, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
38. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 33.
- 25 39. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 33.

40. A method for increasing L-cysteine levels in a cell comprising administering to a subject a sulfhydryl protected cysteine prodrug so as to increase L-cysteine levels in a cell, wherein the prodrug is CySSMA.
- 5 41. The method of claim 40, wherein increasing L-cysteine levels reduces injury caused by an infection, cardiovascular disease, genetic disease, physical injury, ophthalmic disease, cancer, inflammation, neuropathy, exposure to a toxic substance, exposure to ultraviolet light, acute respiratory distress syndrome (ARDS), exposure to radiation and/or decreased levels of glutathione.
- 10 42. The method of claim 40, wherein administration is selected from the group consisting of aerosol, topical, intravenous, intramuscular, subcutaneous, implantable pump, continuous infusion and oral administration.
- 15 43. The method of claim 40, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
44. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 40.
- 20 45. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 40.
46. A method for reducing hepatotoxicity comprising administering to a subject a sulfhydryl protected glutathione prodrug so as to reduce hepatotoxicity.
- 25 47. The method of claim 46, wherein the sulfhydryl protected glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable salt thereof.

48. The method of claim 46, wherein administration is selected from the group consisting of aerosol, topical, intravenous, intramuscular, subcutaneous, implantable pump, continuous infusion and oral administration.
- 5
49. The method of claim 46, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
50. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 46.
- 10
51. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 46.
- 15
52. A method for reducing hepatotoxicity comprising administering to a subject a sulfhydryl protected cysteine prodrug so as to reduce hepatotoxicity, wherein the prodrug is CySSMA.
53. The method of claim 52, wherein administration is selected from the group consisting of aerosol, topical, intravenous, intramuscular, subcutaneous, implantable pump, continuous infusion and oral administration.
- 20
54. The method of claim 52, wherein the subject is selected from the group consisting of human, monkey, dog, cat, cow, sheep, horse, rabbit, mouse, and rat.
- 25
55. A method for prolonging drug therapy by decreasing the toxicity of a drug by the method of claim 52.

56. A method for increasing a therapeutic dosage of a drug by decreasing the toxicity of the drug by the method of claim 52.
- 5 57. A method for reducing hepatotoxicity caused by acetaminophen comprising administering to a subject an effective amount of L-CySSG.
58. A pharmaceutical composition for reducing oxidative stress in a cell comprising a sulfhydryl protected glutathione prodrug and a pharmaceutically acceptable carrier.
- 10 59. The pharmaceutical composition of claim 58, wherein the sulfhydryl protected glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable salt thereof.
- 15 60. The pharmaceutical composition of claim 58, further comprising an agent that can cause cellular oxidative stress.
61. The pharmaceutical composition of claim 59, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.
- 20 62. The pharmaceutical composition of claim 58, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, 25 polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions, tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.

63. A pharmaceutical composition for reducing oxidative stress in a cell comprising a
sulfhydryl protected cysteine prodrug, wherein the cysteine prodrug is CySSMA, and a
pharmaceutically acceptable carrier.
- 5 64. The pharmaceutical composition of claim 63, further comprising an agent that can cause
cellular oxidative stress.
65. The pharmaceutical composition of claim 64, wherein the agent is acetaminophen,
alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.
- 10 66. The pharmaceutical composition of claim 63, wherein the pharmaceutically acceptable
carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins,
such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate,
partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline
15 solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate,
polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions,
tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid
compositions and polymeric compositions.
- 20 67. A pharmaceutical composition for increasing glutathione levels in a cell comprising a
sulfhydryl protected glutathione prodrug and a pharmaceutically acceptable carrier.
68. The pharmaceutical composition of claim 67, wherein the sulfhydryl protected
glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof
25 or a pharmaceutically acceptable salt thereof.
69. The pharmaceutical composition of claim 67, further comprising an agent that can cause
cellular oxidative stress.

70. The pharmaceutical composition of claim 69, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.
- 5 71. The pharmaceutical composition of claim 67, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions, 10 tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.
- 15 72. A pharmaceutical composition for increasing glutathione levels in a cell comprising a sulfhydryl protected cysteine prodrug, wherein the cysteine prodrug is CySSMA, and a pharmaceutically acceptable carrier.
73. The pharmaceutical composition of claim 72, further comprising an agent that can cause cellular oxidative stress.
- 20 74. The pharmaceutical composition of claim 73, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.
- 25 75. The pharmaceutical composition of claim 72, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions,

tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.

- 5 76. A pharmaceutical composition for increasing L-cysteine levels in a cell comprising a sulfhydryl protected glutathione prodrug and a pharmaceutically acceptable carrier.
- 10 77. The pharmaceutical composition of claim 76, wherein the sulfhydryl protected glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable salt thereof.
- 15 78. The pharmaceutical composition of claim 76, further comprising an agent that can cause cellular oxidative stress.
- 15 79. The pharmaceutical composition of claim 78, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.
- 20 80. The pharmaceutical composition of claim 76, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions, tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.
- 25 81. A pharmaceutical composition for increasing L-cysteine levels in a cell comprising a sulfhydryl protected cysteine prodrug, wherein the cysteine prodrug is CySSMA, and a pharmaceutically acceptable carrier.

82. The pharmaceutical composition of claim 81, further comprising an agent that can cause cellular oxidative stress.

83. The pharmaceutical composition of claim 82, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.

84. The pharmaceutical composition of claim 81, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions, tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.

85. A pharmaceutical composition for reducing hepatotoxicity comprising a sulfhydryl protected glutathione prodrug and a pharmaceutically acceptable carrier.

86. The pharmaceutical composition of claim 85, wherein the sulfhydryl protected glutathione prodrug is L-CySSG, GSSMA, GSSME, S-Ac-GSH-OEt, a derivative thereof or a pharmaceutically acceptable salt thereof.

87. The pharmaceutical composition of claim 85, further comprising an agent that can cause cellular oxidative stress.

88. The pharmaceutical composition of claim 87, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.

89. The pharmaceutical composition of claim 85, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions, tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.
90. A pharmaceutical composition for reducing hepatotoxicity comprising a sulfhydryl protected cysteine prodrug, wherein the cysteine prodrug is CySSMA, and a pharmaceutically acceptable carrier.
91. The pharmaceutical composition of claim 90, further comprising an agent that can cause cellular oxidative stress.
92. The pharmaceutical composition of claim 91, wherein the agent is acetaminophen, alcohol, aminoglycoside antibiotic or a chemotherapeutic drug.
93. The pharmaceutical composition of claim 90, wherein the pharmaceutically acceptable carrier is selected ion exchangers, alumina, aluminum stearate, lecithin, serum proteins, such as human serum albumin, buffer substances, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, phosphate buffered saline solution, water, emulsions, salts or electrolytes, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sterile solutions, tablets, excipients, sucrose, glucose, maltose, flavor and color additives, lipid compositions and polymeric compositions.

94. An in vitro method for reducing oxidative stress in a cell comprising contacting the cell with a sulfhydryl protected glutathione prodrug so as to reduce oxidative stress in a cell.
95. The method of claim 94, wherein the sulfhydryl protected glutathione prodrug is CySSG, GSSMA, GSSME or S-Ac-GSH-OEt.
96. An in vitro method for reducing oxidative stress in a cell comprising contacting the cell with a sulfhydryl protected cysteine prodrug so as to reduce oxidative stress in a cell.
97. The method of claim 96, wherein the sulfhydryl protected cysteine prodrug is L-, D- or DL-CySSMA.
98. The method of claim 11, wherein the CySSMA is L- CySSMA, D- CySSMA or DL-CySSMA.
99. The method of claim 27, wherein the CySSMA is L- CySSMA, D- CySSMA or DL-CySSMA.
100. The method of claim 40, wherein the CySSMA is L- CySSMA, D- CySSMA or DL-CySSMA.
101. The method of claim 52, wherein the CySSMA is L- CySSMA, D- CySSMA or DL-CySSMA.
102. The method of claim 72, wherein the CySSMA is L- CySSMA, D- CySSMA or DL-CySSMA.
103. The method of claim 81, wherein the CySSMA is L- CySSMA, D- CySSMA or DL-CySSMA.

104. The method of claim 90, wherein the CySSMA is L- CySSMA, D- CySSMA or DL- CySSMA.